

AD_____

Award Number DAMD17-98-1-8275

TITLE: Institute of Laboratory Animal Research (ILAR)

PRINCIPAL INVESTIGATOR: Ralph Dell

CONTRACTING ORGANIZATION: National Academy of Sciences
Washington, DC 20418

REPORT DATE: March 1999

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are
those of the author(s) and should not be construed as an official
Department of the Army position, policy or decision unless so
designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE March 1999	3. REPORT TYPE AND DATES COVERED Annual (1 Apr 98 - 31 Mar 99)	
4. TITLE AND SUBTITLE Institute of Laboratory Animal Research (ILAR)			5. FUNDING NUMBERS DAMD17-98-1-8275
6. AUTHOR(S) Ralph Dell			
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) National Academy of Sciences Washington, DC 20418		8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES		19990405 027	
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited		12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) The Institute for Laboratory Animal Research (ILAR) is a component of the Commission on Life Sciences (CLS), National Research Council (NRC). Partial support for ILAR has been provided for many years from the Department of the Army to enable ILAR to fulfill its mission. Founded in 1952, ILAR has become recognized nationally and internationally as a leader in developing and making available to the biomedical and laboratory animal science communities guidelines for animal care, breeding, and use; descriptions of animal models for human diseases and physiological processes; and reports on specific issues of humane care and use of laboratory animals. ILAR's mission is to help improve the availability, quality, care, and humane and scientifically valid use of laboratory animals.			
ILAR accomplishes its goals through its core program, which is carried out by the staff, and its special-project program, which is carried out by NRC-appointed committees with staff assistance. The number of committees and size of the staff are dependent on the number of special projects and available funding. Both programs are directed by a 14-member Council comprised of experts in laboratory animal medicine, zoology, genetics, medicine, ethics, and related biomedical sciences. The Army funds partially support general office operations, the Animal Models and Genetic Stocks Information Program, publication of <i>ILAR Journal</i> , and work of the Council.			
14. SUBJECT TERMS ILAR, guidelines, animals, animal models, medical research			15. NUMBER OF PAGES 13
			16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

Where copyrighted material is quoted, permission has been obtained to use such material.

Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

Maya Deel 3/11/99
PI - Signature Date

Abstract

The Institute for Laboratory Animal Research (ILAR) is a component of the Commission on Life Sciences (CLS), National Research Council (NRC). Partial support for ILAR has been provided for many years from the Department of the Army to enable ILAR to fulfill its mission.

Founded in 1952, ILAR has become recognized nationally and internationally as a leader in developing and making available to the biomedical and laboratory animal science communities guidelines for animal care, breeding, and use; descriptions of animal models for human diseases and physiological processes; and reports on specific issues of humane care and use of laboratory animals. ILAR's mission is to help improve the availability, quality, care, and humane and scientifically valid use of laboratory animals.

ILAR accomplishes its goals through its core program, which is carried out by the staff, and its special-project program, which is carried out by NRC-appointed committees with staff assistance. The number of committees and size of the staff are dependent on the number of special projects and available funding. Both programs are directed by a 14-member Council comprised of experts in laboratory animal medicine, zoology, genetics, medicine, ethics, and related biomedical sciences. The Army funds partially support general office operations, the Animal Models and Genetic Stocks Information Program, publication of *ILAR Journal*, and work of the Council.

INTRODUCTION

For many years the Army has provided partial core support to the Institute for Laboratory Animal Research (ILAR), a component of the National Research Council's (NRC) Commission on Life Sciences. The NRC is the operating arm of the National Academy of Sciences, a private, nonprofit organization that was created in 1863 by congressional charter to serve as an official advisor to the federal government on questions of science and technology.

Founded in 1952, ILAR has become recognized nationally and internationally as a leader in developing and making available to the biomedical and laboratory animal science communities guidelines for animal care, breeding, and use; descriptions of animal models for human diseases and physiological processes; and reports on specific issues of scientific and humane use of laboratory animals. These guidelines from the National Academy of Sciences serve as important indications to members of congress, government officials, the press, and the public of the high quality of care provided to laboratory animals. ILAR's mission is to help improve the availability, quality, care, and humane and scientifically valid use of laboratory animals.

ILAR's studies, like all those of the NRC, are carried out by recognized experts in fields appropriate to the required tasks. These serve on a volunteer basis, without compensation. As a part of the NRC, ILAR has access to this country's most knowledgeable and distinguished laboratory animal and biomedical scientists, who provide objective counsel on laboratory animal matters. A significant number of the experts used by ILAR are also members of the National Academy of Sciences or the Institute of Medicine. In some cases, ILAR utilizes scientists from other countries.

Reports of NRC studies are extensively reviewed by independent NRC-appointed experts in the subject area before they are released. They are prepared in sufficient quantity to ensure distribution to the sponsor, experts, and other relevant parties in accordance with Academy policy. Reports are usually made available to the public without restriction.

ILAR'S GOALS

- Since its founding, ILAR has provided guidance and information on laboratory animal matters to the federal government, the biomedical and laboratory animal science communities, and the public. In keeping with its mission, ILAR continually seeks to strengthen and refine its existing programs and to initiate new programs that will assist government officials; scientists who use animals in research, testing, and education; and the institutional animal care and use committees that monitor animal use. ILAR's goals are as follows:
- to provide a forum within the National Academy of Sciences for the Department of Defense to discuss issues and develop guidance for laboratory animal-related matters;

- to continue to serve on behalf of biomedical science and education as an authoritative voice within the U.S., and on behalf of the U.S. scientists internationally;
- to promote humane and appropriate care and use of laboratory animals;
- to provide scientific guidance on laboratory animal-related issues to agencies of the federal government and others on request;
- to provide information on laboratory animal matters to government officials, laboratory animal and other biomedical scientists, institutional animal care and use committees, and the public;
- to promote the use of standardized nomenclature for accurately defining and identifying genetic stocks of animals;
- to assist developing countries attain quality laboratory animal science programs through dissemination of information including the translation of ILAR reports;
- to promote cost-effective ways to preserve valuable animal models; and
- to broaden the access to information on selection of appropriate biological models and methods through ILAR's home page, databases, publications, and resources of the new ILAR Associateship program.

Accomplishing the Goals

ILAR accomplishes its goals through its core program, which is carried out by the staff, and its special-project program. The number of studies and size of the staff are dependent on the number of special projects and available funding. Both programs are directed by a 16-member ILAR Council comprised of experts in laboratory animal medicine, virology, zoology, genetics, medicine, ethics, and related biomedical sciences.

THE CORE PROGRAM

ILAR Council

The ILAR Council (see addenda for roster) serves four principal functions: to provide program direction and strategic planning; to oversee the information programs, which consist of the Animal Models and Genetic Stocks Information Program and the quarterly *ILAR Journal*; to oversee special projects; and to direct ILAR's international programs and its participation as the U.S. national member in the International Council of Laboratory Animal Sciences (ICLAS). The international program is discussed in the Special Projects section below. Periodically, the Council meets with other scientists and funding agency administrators to discuss areas in which ILAR might prove useful. It then uses these discussions in strategic planning. The Council occasionally employs core funds to undertake specific, NRC-approved projects itself.

Staff

ILAR is staffed by a director, a managing editor of the *ILAR Journal*, a project assistant who maintains the AMGS database, a project assistant and secretary to the director, and a project director (currently vacant). Under the special projects program, staff works closely with experts to engage in studies, develop working papers, assist in the production of a cohesive report, and conduct literature reviews.

Animal Models and Genetic Stocks Information Program

Some of the most critical information needed by Department of Defense scientists is often the most difficult to obtain, including information on the most appropriate model for the proposed research and, if the model is an animal, to find sources of the model and information on appropriate care. As author of the *Guide for the Care and Use of Laboratory Animals*, ILAR is in a position to assist investigators and Institutional Animal Care and Use Committees (IACUCs) in interpreting guidelines for the humane care and use of animals and fulfilling requirements of the Animal Welfare Regulations regarding reduction of pain and distress and identification of alternative methodologies. For over 40 years, ILAR has conducted a program to provide such information. That program, called the Animal Models and Genetic Stocks Information Program, offers assistance in locating sources of animals, selecting appropriate animal models, using standardized nomenclature, and understanding the importance of the use of animals in biomedical and behavioral research and testing. It includes two databases: one (called Animals for Research, AFR) contains commercially available and investigator-held colonies of animals for research; the other is a registry of codes used with standardized nomenclature of rodents and rabbits to identify institutions that maintain breeding colonies. The databases have been incorporated into ILAR's World Wide Web (WWW) home page and are available to investigators world-wide. The Animals for Research website averages approximately 10 "hits" per day. ILAR has just undertaken a major update to both databases and expects to add many new sources as well as increased information about the animal stocks listed.

ILAR Journal

ILAR Journal, a quarterly, peer-reviewed publication, provides thoughtful and timely information for all those who use, care for, and oversee the use of laboratory animals. The audience of *ILAR Journal* includes more than 3,500 investigators in biomedical and related research, institutional officials for research, veterinarians, and members of animal care and use committees. The *ILAR Journal* Editorial Board, of the ILAR Council, plans each issue around a chosen theme and carefully solicits authors to best present a balanced view of the topic which is then peer reviewed.

The hiring of a full-time editor for *ILAR Journal* has made the past year a very productive one. During the last year (March 1998 to February 1999), ILAR has published six Journal issues (see reference list) on the following themes: Animal Models of Aging Research; Understanding and Using the Internet and the World Wide Web; Animal Well-being: Immune Function, Behavior, Morphology, and Psychoneuroimmunology; Comparative Gene Mapping (a very large, double

issue comprising 22 articles devoted to different species and including two large color posters); and Opportunistic Infections in Laboratory Rats and Mice. In March and April 1999, issues devoted to Bioethics of Laboratory Animal Research and Animal Models of Human Vision will be published.

Forthcoming issues in various stages of production are devoted to Animal Models of Nociception, Squirrel Monkeys in Biomedical and Behavioral Research, Behavior of the Laboratory Mouse, Animal Models of Inflammation, Humane Endpoints of Toxicity, and Animal Models of Cryobiology. Ideas for future issues include Animal Models of Hepatitis B and/or C, Studies of Antibiotic Resistance, History and Future of Chimpanzees or Old World Primates, Genetic Management (with a possible focus on Macaques or Rhesus and Cynomolgus Monkeys), Occupational Health and Nonhuman Primates, and Laboratory Animal Allergens.

ILAR Associate Program

In an effort to provide better access to ILAR's information and resources and to better leverage funding from core and project sponsors, ILAR initiated an associateship program in 1997. Individuals and institutions who subscribe to the associate program help defray the cost of publishing the *Journal* and managing the AMGS program. ILAR Associates receive the *ILAR Journal* (number of copies varies with level of Associate membership), expedited and individualized responses from the AMGS program, and receive a 20% discount on all ILAR publications, as well as all publications of the National Academy Press. As do ILAR's core sponsors, the Associates arguably represent the best of U.S. biomedical and laboratory animal scientists and serve as an important audience to receive, critique, and provide guidance to ILAR's programs. ILAR's core sponsors are valuable members of the Associates program.

SPECIAL PROJECTS

Projects are developed in response to specific requests from government agencies and private organizations or on the initiative of staff, or ILAR Council. Although these projects are supported by contracts and grants from federal agencies, foundations, and private organizations, they are never completely separate from the core program because the Council is involved during each step of the process. This sponsorship provided by this grant is recognized in each published ILAR report. The Council reviews each project extensively before it is undertaken, examines, the qualifications of experts, oversees the conduct of the project to ensure that it is accomplished in a timely manner, and reviews and signs off on each report as a part of the NRC review process. In addition, ILAR reports are frequently published as special inserts of the core-support *ILAR Journal*. The following projects are examples of recently completed projects, or projects that are underway or which will begin when funding has been received.

ICLAS and International Activities

ILAR has had a long history of interest in international laboratory animal science. Historically, this interest has sought to assist young investigators in developing countries through dissemination of reports (some translated into foreign languages to increase their usefulness) and participation in international meetings that support young investigators. In 1988, ILAR became the U.S. national member of the International Council for Laboratory Animal Science (ICLAS), with support from member agencies (including USAMRDC) of the Interagency Research Animal Committee (IRAC). This membership affords a conduit for U.S. investigators to develop and conduct an active international program in laboratory animal science. One goal of the U.S. membership in ICLAS was to streamline ICLAS management and programs to better represent U.S. scientists in the international community. In 1995, that goal came to fruition through the election of former ILAR Council chairman (Steven Pakes) as Secretary General of the ICLAS General Assembly. Dr. Pakes works closely with ILAR and is an annual guest of ILAR Council to discuss ICLAS and other international issues.

The goals of ILAR's international activities center around the following:

- Facilitating the impact of NAFTA for the benefit of trade affecting scientific exchange
- Developing a database of contacts (scientists, government officials, and trade organizations) in Mexico and Canada
- Updating and expanding ILAR's online database on Animals for Research
- Distribution of NRC reports to appropriate scientific audiences
- Translation of Reports

In the past year ILAR's *Guide for the Care and Use of Laboratory Animals* has been translated into Chinese, Korean, and Japanese. Ones in Spanish, French, and Russian are nearly completed. The Spanish translation will be distributed by the Mexican National Academy of Medicine. The use of the *Guide* internationally by scientists and laboratory animal personnel further supports ILAR's effort to achieve animal care and use policies that will facilitate international scientific exchange of biologics and products.

A meeting was held at the end on October 23, 1998 to discuss the need for microbiologically and genetically defined mice and rats, definitions which would facilitate the sharing of information between the Japan and the US. Annual US/Japan meetings have been occurring since 1980 and have resulted in a number of notable efforts including several ILAR publications. The meetings were held at NIH but the unit which organized and hosted the meeting no longer exists due to NIH reorganization. So it seemed logical for ILAR to become the home of this annual meeting since ILAR have been intimately involved in the meetings for years. The proceedings of this meeting will be published as part of one of the ILAR Journal issues.

Workshop on Pain Management and Human Endpoints

A workshop on Pain Management and Human Endpoints was held on November 2, 1998. It focused on the science, ethics, assessment and alleviation of pain, stress and distress in animals involved in research. The agenda and the papers presented at the workshop can be seen at the website www.altweb.jhsph.edu. The workshop was cosponsored by ILAR, the Center for Alternatives to Animal Testing, and the Humane Society of the United States.

Workshop on Rats, Mice, and Birds

On February 2, 1999 a workshop on Rats, Mice and Birds was held. This workshop was held in connection with the Scientific Scientists Center for Animal Welfare and focused on the advantages, disadvantages, and other features of regulating the care and use effects of including rats, mice, and birds under provisions of the Animal Welfare Act. Interested parties and organizations presented views on the possibility of such regulations for the purpose of furthering an objective, science-based dialog in order to inform policy decision-making the possible regulatory burden, the need for USDA not to decrease inspections of species of animals now covered, and the need for USDA to receive more money for the extra inspections if they decide to include rats, mice, and birds under the regulations.

The Psychological Well-Being of Nonhuman Primates

The report of this project was published by the National Academy Press in June 1998. The report recommends practical approaches to meeting the requirement of the 1985 amendment to the Animal Welfare Act, which requires those who keep nonhuman primates to develop and follow appropriate plans for promoting the animals' psychological well-being. It focuses on what is known about the psychological needs of primates and makes suggestions for assessing and promoting their well-being.

The Cost of Animal-Based Research

This study supported by NIH was initiated in September 1997 and has two related tasks: to examine the cost allocation method described in the revised NIH Rate Setting Manual, compare that method to the allocation scheme called for in OMB Circular A-21 and make recommendations concerning cost allocation; and secondly, to examine the components of the total cost of using animals in research and determine what cost containment strategies might be considered. The interim report on the cost allocation issue was completed and released in May 1998. The final report is expected by the summer of 1999.

Methods for Producing Monoclonal Antibodies

Monoclonal antibodies are used extensively in medical and biological research as reagents to detect and quantitate various proteins and other substances in cells and body fluids and as

therapeutic agents in cancer research. A study was initiated in September 1998 with support from NIH to examine the scientific need to use the mouse ascites method for producing monoclonal antibodies and if the committee decides it is necessary, then to recommend ways of minimizing pain and distress in the mice. The report has been completed and is in press; a prepublication will be released by March 31, 1999.

Prospective Activities

- The Behavior of the Laboratory Mouse--A workshop will be held to summarize current knowledge concerning behavioral research on the laboratory mouse. An earlier ILAR report entitled *Biomedical Models and Resources* described the need for researchers to have behavior as a variable when characterizing the phenotype of genetically altered mice.
- Occupational Health and Safety in Care of Nonhuman Primates—A committee will be asked to identify the hazards associated with using nonhuman primates (NHPs) in research, assess the degree of risk of these hazards, and suggest options for managing the risks including engineering controls, personal protective equipment, and worker training. Recommendations would be made for institutional management of workers after suspected exposure.
- Revision of *Science, Medicine, and Animals*. A subcommittee of ILAR would review and prepare a revision of the 1991 publication, *Science, Medicine, and Animals*. The revision would use more modern examples of the benefits of the use of animals in research and would serve as an educational and informational document to provide a scientific discussion of continually evolving and unsettled issues associated with animal use in research. An extensive dissemination effort would be carried out that would include targeted mailings, briefings, seminars, educational exhibits at scientific and professional meetings.
- The 1978 ILAR report entitled *Laboratory Animal Housing* will be updated using modern technical criteria for animal research facility design including performance criteria, description of the animal environment, requirements for hazardous agent containment, cost-effectiveness of design for new construction as well as renovation.

REFERENCES

1. Institute for Laboratory Animal Research. 1997. *ILAR Journal* 38(3): 102-159.
2. Institute for Laboratory Animal Research. 1997. *ILAR Journal* 38(4):160-196.
3. Institute for Laboratory Animal Research. 1998. *ILAR Journal* 39(1). 1-44.
4. Institute for Laboratory Animal Research. 1998. *ILAR Journal* 39(2&3). 45-260.
5. Institute for Laboratory Animal Research. 1998. *ILAR Journal* 39(4). 261-335.
6. National Research Council. 1998. *The Psychological Well-Being of Nonhuman Primates*. National Academy Press, Washington, D.C. 168 pp.
7. National Research Council. 1998. *Approaches to Cost Recovery for Animal Research: Implications for Science, Animals, Research Competitiveness, and Regulatory Compliance*. (Interim report of the Committee on Cost of and Payment for Animal Research)
8. National Research Council. In Press. *Monoclonal Antibody Production*. National Academy Press, Washington, D.C.

March 1999

INSTITUTE FOR LABORATORY ANIMAL RESEARCH COUNCIL MEMBERS

John L. VandeBerg, Ph.D. (*Chairman*)
Southwest Foundation for Biomedical Research
(Biochemical Genetics, Mammalogy)

Christian Abee, D.V.M.
Department of Comparative Medicine
University of South Alabama
(Laboratory Animal Medicine)

Bennett Dyke, Ph.D.
Southwest Foundation for Biomedical Research
(Biological Database Management)

Rosemary W. Elliott, Ph.D.
Department of Molecular and Cellular Biology
Roswell Park Cancer Institute
(Molecular Cell Biology)

Gerald F. Gebhart, Ph.D.
Department of Pharmacology
University of Iowa
(Laboratory Animal Medicine)

Hilton J. Klein, V.M.D.
Department of Laboratory Animal Resources
Merck Research Laboratories
(Laboratory Animal Medicine)

Margaret Landi, V.M.D.
SmithKline Beecham Pharmaceuticals
Department of Laboratory Animal Science
(Laboratory Animal Medicine)

Charles McCarthy, Ph.D.
Kennedy Institute of Ethics
Georgetown University
(Ethics)

Harley Moon, D.V.M.
Veterinary Medical Research Institute
Iowa State University
(Veterinary Pathology)

William Morton, V.M.D.
Regional Primate Research Center
University of Washington
(Primateology)

Robert J. Russell, D.V.M.
Harlan Sprague Dawley, Inc.
(Laboratory Animal Medicine)

William S. Stokes, D.V.M.
Animal Alternative Research
National Institute of Environmental Health Science
(Alternatives in Animal Testing)

John G. Vandenbergh, Ph.D.
Department of Zoology
North Carolina State University
(Reproductive Biology, Rodents, Primates,
Nontraditional Animals)

Peter Ward, M.D.
Department of Pathology
University of Michigan
(Pathology)

Thomas Wolfle, Ph.D., D.V.M.
Consultant
Annapolis, MD
(Primatology)

Joanne Zurlo, Ph.D.
Center for Alternatives to Animal Testing
Johns Hopkins School of Hygiene and Public Health
(Alternatives in Animal Testing)